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Inventors: Laurencin et al.
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REMARKS

Claims 1-11 are pending in the instant application. Claims 1-11 have been rejected. Claims 1 and 2 have been amended. Support for these amendments is provided throughout the specification and in particular at page 1, lines 14-15, page 4, lines 6-9, page 5, lines 32-33 and page 9, lines 22-31. Thus, no new matter has been added by these amendments. Reconsideration is respectfully requested in light of these amendments and the following remarks.

I. Rejection of Claims 1 and 8-11 under 35 U.S.C. § 103(a)

Claims 1 and 8-11 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Vacanti et al. in view of Hlavacek et al. The Examiner has acknowledged Vacanti et al. to be "silent" with respect to a braided scaffold. However, the Examiner suggests that Hlavacek et al. teaches a three-dimensional scaffold that is braided. Thus, the Examiner suggests that it would have been obvious to one of ordinary skill in the art at the time of applicants' invention to look at the teachings of Hlavacek et al. to make the degradable, porous, polymeric fiber based-three dimensional scaffold of Vacanti et al. braided to impart the desired strength and stiffness in the primary axial loading direction.

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Applicants respectfully disagree.

The term "three-dimensional" as used in the instant invention and made clear by the teachings of the specification at, for example page 5 and 6, refers to the textile structure of the braid and not to the dimensions of the object as a whole. Neither Vacanti et al. nor Hlavacek et al. teach a braided three-dimensional textile structure. Instead, Vacanti et al. discloses a two-dimensional textile structure "in a woven or non-woven mesh and sponge like device" (column 3, line 51) while Hlavacek et al. discloses "devices that are braided or woven into flat tape geometry having the plurality of fibers aligned parallel to form the axial warp."

Accordingly, in an earnest effort to clearly distinguish the three-dimensional textile structures of the present invention from the two-dimensional textile structures of Vacanti et al. and Hlavacek et al., Applicants have amended the claims to state that the three-dimensional braided scaffolds are formed using a three-dimensional textile braiding technique. Support for this amendment is provided in the specification at page 5, lines 32-33.

Further, it has been shown in the literature that two-dimensional textile structures, such as described by Vacanti et

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al. and Hlavacek et al. fail as ligament or tendon replacement constructs. Applicants are providing herewith a reference by Guidoin et al. (Biomaterials 2000 21:2461-2474) which describes the failures of two-dimensional polymeric fiber-based replacements for ACL and textile structures similar to Hlavacek et al. Accordingly, to further distinguish the present invention from such two-dimensional replacement constructs, Applicants have amended the claims to clarify that the replacement construct are for tendons or ligaments. Support for this amendment can be found in the specification at page 1, lines 14-15, page 4, lines 6-9, and page 9, lines 22-31.

Finally, Applicants would like to clarify that the major forces placed on a ligament are flexural and rotational loading. Accordingly, the Examiner's suggestion that one of skill would look to Hlavacek et al. to impart the desired strength and stiffness in the primary axial loading direction to the constructs of Vacanti et al. is irrelevant to ligament and tendon replacement constructs of the present invention.

Accordingly, the combination of Vacanti et al. and Hlavacek et al. does not teach or suggest all the limitations of the claims as amended. Specifically, neither of these references

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teach or suggest three-dimensional braided scaffolds formed using a three-dimensional textile braiding technique.

The combination of Vacanti et al. and Hlavacek et al. also fails to provide any reasonable expectation of success of the claimed constructs in ligament and tendon replacement, particularly in light of literature references such as Guidoin et al. reporting failure of two-dimensional constructs such as taught by Hlavacek et al. for ACL replacement.

Finally, there is no motivation to combine the teachings of Vacanti et al. with Hlavacek et al. to produce a ligament or tendon replacement construct since the additional strength suggested by the Examiner to be obtained is irrelevant to ligament and tendon replacement constructs.

Thus, since this combination of references fails to meet the basic criteria required for a *prima facie* case of obviousness, it is respectfully requested that the rejection of claims 1 and 8-11 over the teachings of Vacanti et al. and Hlavacek et al. be withdrawn.

II. Rejection of Claims 2-7 under 35 U.S.C. § 103(a)

Claims 2-7 have also been rejected under 35 U.S.C. § 103(a) as being unpatentable over Hlavacek et al. in view of Vacanti et al. The Examiner suggests that Hlavacek et al. discloses a

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braided ligament or tendon implant with all the elements of claim 2, but is silent with respect to seeding with cells. However, the Examiner suggests that Vacanti et al. teaches a replacement construct seeded with cells. Thus, the Examiner suggests that it would have been obvious to one of ordinary skill in the art at the time of applicants' invention to look at the teachings of Vacanti et al. to modify the ligament or tendon implant of Hlavacek et al. to seed the polymeric scaffold with cells.

Applicants respectfully traverse this rejection.

As discussed in Section I, *supra*, contrary to the Examiner's suggestion, Hlavacek et al. does not teach a braided ligament or tendon implant with all the elements of the instant invention. Specifically, neither Hlavacek et al. nor Vacanti et al. teach three-dimensional braided scaffolds formed using a 3-dimensional textile braiding technique.

Accordingly, in an earnest effort to clearly distinguish the instant invention from the teachings of the cited prior art references, Applicants have amended claim 2 to state that the three-dimensional braided scaffolds are formed using a three-dimensional textile braiding technique. Support for this amendment is provided in the specification at page 5, lines 32-33.

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Further, as also discussed in Section I, *supra*, the literature has disclosed that two-dimensional textile structures such as described by Vacanti et al. and Hlavacek et al. fail as ligament or tendon replacement constructs. Accordingly, to further distinguish the present invention from such two-dimensional replacement constructs, Applicants have amended claim 2 to clarify that the replacement constructs are for tendons or ligaments. Support for this amendment can be found in the specification at page 1, lines 14-15, page 4, lines 6-9, and page 9, lines 22-31.

These amendments to independent claim 2, which clearly distinguish the claimed invention from teachings of the combination of Hlavacek et al. and Vacanti et al., render moot the Examiner's additional comments with respect to dependent claims 3-7, since MPEP § 2143.03 makes quite clear that if an independent claim is nonobvious under 35 U.S.C. § 103, then any claim depending therefore is nonobvious.

Thus, since the cited prior art references do not teach or suggest all the limitations of claims 2-7 as amended, nor provide a reasonable expectation of success with respect to use of the claimed invention in ligament or tendon replacement, withdrawal

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of the rejection of claims 2-7 under 35 U.S.C. § 103 is respectfully requested.

III. Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,

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Analysis of retrieved polymer fiber based replacements for the ACL

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Abstract

The present retrospective analysis of 117 surgically excised anterior cruciate ligament (ACL) prostheses was designed to elucidate the etiology and mechanisms of failure of synthetic ligamentous prostheses. They were harvested from young and active patients (26 ± 7 yrs) at various orthopaedic centers in France between 1983 and 1993. The average duration of implantation of augmentation and replacement prostheses were 21.5 ± 12.6 and 33.2 ± 25.3 months, respectively. The principal causes for their excision were ruptures and synovitis. Each ACL prosthesis was examined macroscopically, histologically, and, after tissue removal, by scanning electron microscopy (SEM) to determine the model, manufacturer, surgical technique used at implantation, the extent of healing, the site of rupture, and the morphology of the damaged fibers. Fourteen types of ACL prostheses were analysed, each fabricated using a different combination of polymers, fibers and textile constructions. Consequently, they generated a variety of healing characteristics and mechanical responses in vivo. SEM observations revealed that abrasion of the textile fibers as a result of yarn-on-yarn and/or yarn-on-bone contact was a common phenomenon to almost all models, and was the primary cause of prosthetic failure. Healing inside the synthetic ACL was poorly organized, incomplete and unpredictable as the extent of collagenous infiltration into the textile structure did not increase with the duration of implantation. In fact, the collagenous infiltration into certain models appeared to be more detrimental than beneficial since it caused deterioration and fraying of the textile structure rather than serving as a reinforcing matrix around the prosthesis. In conclusion, the present study shows that three mechanisms may be involved in the failure of ACL prostheses: (1) inadequate fiber abrasion resistance against osseous surfaces; (2) flexural and rotational fatigue of the fibers, and (3) loss of integrity of the textile structure due to unpredictable tissue infiltration during healing. © 2000 Elsevier Science Ltd. All rights reserved.

Keywords: ACL prostheses: Retrieval study: Histology; SEM analysis

1. Introduction

The anterior cruciate ligament (ACL) is an important part of the knee which maintains the stability and the function of the organ. If treated conservatively, rupture of the ACL may lead to knee instability, osteoarthritis, and meniscal tears [1,2]. During the 1970s, autogenous tissue and heterografts were popular substitutes. However, the risks of surgically transmitted infectious diseases, such as hepatitis or HIV, the weakening of adjacent anatomical tissue and the amount of tissue available for ACL reconstruction have convinced orthopedic surgeons of the utility of an artificial substitute [3–5].

Over the years, only a few companies have developed useful prosthetic devices. In 1973, the Food and Drug Administration (FDA) approved the first Proplast® device, and by the mid-1970s, the original Kennedy prosthesis made from Hercules® 1900 ultra-high-molecular weight polyethylene also known as high-performance polyethylene (PHP), became commercially available. Thereafter, Jenkins et al. introduced a prosthesis made from carbon [6] and the Kennedy-Lad® augmentation device began to be implanted for the reinforcement of a torn or injured ligament. The Leeds-Keio®, the Gore-Tex® and the Stryker® prostheses emerged along with other prototypes during the 1980s [7].

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The introduction of these ligamentous prostheses generated much interest because it offered the benefit of quick recovery and rapid rehabilitation of the knee without sacrificing the autogenous tissue [8]. While preliminary studies showed promise, long-term results were disappointing with success rates ranging between 30 and 60% [9–14]. A number of problems were reported, including elongation and rupture of the device, synovitis, bone tunnel enlargment, lack of sensibility, and the formation of wear debris [15–17]. After a number of trials, it was finally recommended to cease the use of these devices [18]. Nowadays, autogenous and allogenic tissue, such as the patellar tendon, semi-tendinous tendon, fascia lata, and the iliotibial band, as well as techniques related to tissue harvesting and implantation procedures, have contributed to improving the success rate of ACL repair [19–24].

As the use of ligamentous prostheses did not appear to solve the problem of ACL rupture, and since the long-term results were disappointing, the question to be answered is: 'Do we still need an artificial substitute to replace or reinforce a broken or torn ACL?' If the answer is 'Yes', then before beginning new programs for the development of an ACL prosthesis, it is important that we understand why they failed.

The present study was undertaken with the purpose of addressing this issue. A large number of synthetic ACL grafts which had failed prematurely were retrieved and analyzed histologically and morphologically with a view to identifying the most common mechanisms of clinical failure.

2. Materials and methods

2.1. Prostheses

One hundred and seventeen (117) explanted ACL ligamentous prostheses and augmentation devices were harvested at various centers in France and in Canada from 1987 to 1996. Fifteen different types of retrieved grafts were received at the Quebec Biomaterials Institute including 28 Stryker®, 22 Proflex®, 13 Lygeron®, 12 Kennedy-LAD®, 7 ABC Surgicraft® polyester (polyethylene terephthalate) (PET), 7 Ligastic®, 6 SEM®, 6 Raschel PHP®, 6 braided PHP®, 4 Ligaid®, 3 Gore-Tex®, and 2 ABC Surgicraft® PET/carbon devices. One prosthesis was not identified. Table 1 lists the name of the manufacturer, the type of the textile structure and the type of synthetic fibers used in the construction of each device.

2.2. Clinical data

Surgeons participating in the retrieval program were asked to complete a data sheet upon explantation of the prosthesis. A summary of each patient's file was required in order to generate a profile of the patient population, determine the reasons for the original injury to the natural ACL, identify the type of prosthesis and identify the surgical technique used for implantation.

2.3. Graft harvesting

After excision, each prosthesis was carefully rinsed in saline, placed in a buffered solution of glutaraldehyde and shipped to Quebec City for further analysis. On reception, each prosthesis was either placed on a horizontal transparent glass plate or mounted on a plastic knee for macroscopic examination using a Tessovar macroscopic zoom system (Zeiss, Oberkochen, Germany). The type of prosthesis, the manufacturer, the degree of encapsulation, the site of rupture, and the surgical technique used at implantation were observed and recorded. A graduated ruler was used to measure the length of each segment and to localize the region where the maximum mechanical damage occurred.

2.4. Histopathological study

Representative specimens from each prostheses were cut in sections of approximately 5 mm × 5 mm. Each of these sections were postfixed in 10% formalin, dried in solutions of increasing concentration of toluene and ethanol and then embedded in paraffin wax. Five micron thick sections were stained with hematoxylin–phloxine–safran and Masson's trichrome to visualize the cellular response and collagen synthesis, respectively. Histological examination included the evaluation of various healing parameters, such as the phase and the severity of the inflammatory reaction, the different types of inflammatory cells present, the degree of encapsulation and penetration of collagen into the prosthetic structure, and the severity of any infection if reported by the surgeon.

2.5. Scanning electron microscopy study

Further analysis consisted of observing the extent of damage to the textile structure and identifying, where possible, the failure mechanism for each ACL prosthesis. The most significantly damaged segment of each prosthesis was cleaned of all adhering tissue by treating with 5% sodium bicarbonate solution at the boil for 5 min, followed by a 24 h immersion at room temperature. After rinsing with deionized water, they were placed in two successive baths of 5% sodium hypochlorite bleach solution for 2 h, rinsed thoroughly in distilled water and dried. Representative specimens were removed from locations near the sites of wear and breakage. They were then post-fixed in a 1% aqueous solution of osmium tetroxide, rinsed in water, dehydrated by immersion in a series of aqueous solutions of increasing ethanol

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Table 1
Description of the prostheses received between 1983 and 1993[a]

Commercial name	Biomedical company	Description	Material	Number
Stryker®	Stryker, USA	4–6 woven tapes in a tubular shell	PET/PP	28
Proflex®	Protek, France	15 concentric tubular braids of 32 yarns	PET	22
Lygeron®	Orthogroup, France	6 ribbons in a woven tube	PET	13
Kennedy-LAD®	3M, USA	Braided narrow ribbons	PP	12
ABC® Surgicraft	Surgicraft, UK	24 braided narrow ribbons wrapped at ends	PET	8
Ligastic®	Orthomed, France	Rolled tricot knit into a tubular shape with a polyurethane shell	PET	7
SEM®	Science et Médecine, France	Two concentric tubular braids	PET	6
Raschel®	Cendis Médical, France	Knitted structure rolled into tubular shape	UHMWPE	6
Braided PEP	Cendis Médical, France	Double concentric tubular braids	UHMWPE	6
Ligaid®	Proth-Aid, France	Twisted cords braided wrapped at ends	PAA	4
Gore-Tex®	W.L.Gore and Associates, USA	24 braids of 3 yarns wrapped at ends	PTFE	3
ABC® Surgicraft	Surgicraft, UK	24 braided narrow ribbons wrapped at ends	PET/C	2

[a]PET = polyester; PP = polypropylene; UHMWPE = ultra-high-molecular weight polyethylene; PAA = polyarylamide; PTFE = polytetrafluoroethylene.

concentration and dried with hexamethyldisilazane. Samples were finally vacuum coated with gold–palladium and examined in a JSM 35CF Jeol scanning electron microscope (Soquelec, Montréal, QC, Canada) at 15 kV accelerating voltage.

3. Results

3.1. Patients and clinical information

The 117 explants were harvested from 74 males, 29 females and 14 patients of unknown sex. The mean age of these patients at the time of implantation was 25.6 ± 6.7 yrs (Fig. 1). Injury to their natural ACL occurred as a result of sports injuries in 87.5% of the cases ($n = 72$) (Fig. 2). Fig. 3 shows a wide and skewed distribution of the duration of implantation for the various prostheses. Table 2 also provides evidence of a wide divergence of implantation times for those ligamentous prostheses made from polyester fibres.

3.2. Augmentation devices

Twelve polypropylene Kennedy-LAD® augmentation devices were retrieved and evaluated. The mean age of the patients at the time of implantation was 23 ± 5 yrs ($n = 11$) and the mean duration of implantation was 21.5 ± 13.2 months ($n = 11$). In five cases out of the 12, only one end had been retrieved and submitted for analysis. In fact, only one prosthesis was complete. Examination of the medical reports revealed that the McIntosh technique using the semi-tendinous tendon was preferred ($n = 4$) to the use of fascia-lata, patellar tendon or the quadriceps when performing the operation. The thickness of collagen varied along the length of the prostheses. At histology, the healing of the Kennedy-LAD® augmentation device was characterized by the development of a thin collagenous capsule with limited collagen infiltration into the prosthetic structure, even after more than 3 yrs of implantation. The inflammatory response was mild.

The SEM examination showed that even if the segment that had been located in the tibial tunnel was well preserved, there was significant yarn-on-yarn abrasion at the distal end of the explant and at the anchorage site as well as yarn-on-bone abrasion at the exit to the tunnel. The typical characteristic that indicated abrasion was surface peeling of individual fibers. Compressed fibres were also present. Iatrogenic damage was also observed. It was most probably caused by difficulties at harvesting.

3.3. Replacement ligaments

3.3.1. Polyester ligaments

Stryker® ligaments: The 28 prostheses received at the IBQ were implanted between 1983 and 1990. Macroscopic observations showed that the over-the-top technique was used more frequently than the through-the-condyle approach. In four cases, the surgical technique could not be discerned because of the extent of damage to the devices. Prostheses inserted using the over-the-top technique were well preserved in the tibial tunnel, but fiber separation, fraying and signs of abrasion of the external shell were evident in the intra-articular region. Rupture of the prosthesis generally occurred at the distal end of the tibial tunnel or in the intra-articular zone (Fig. 4). The ruptured sites of the through-the-condyle technique were localized either at the tibial plateau or above the condyle. The intra-articular zone was

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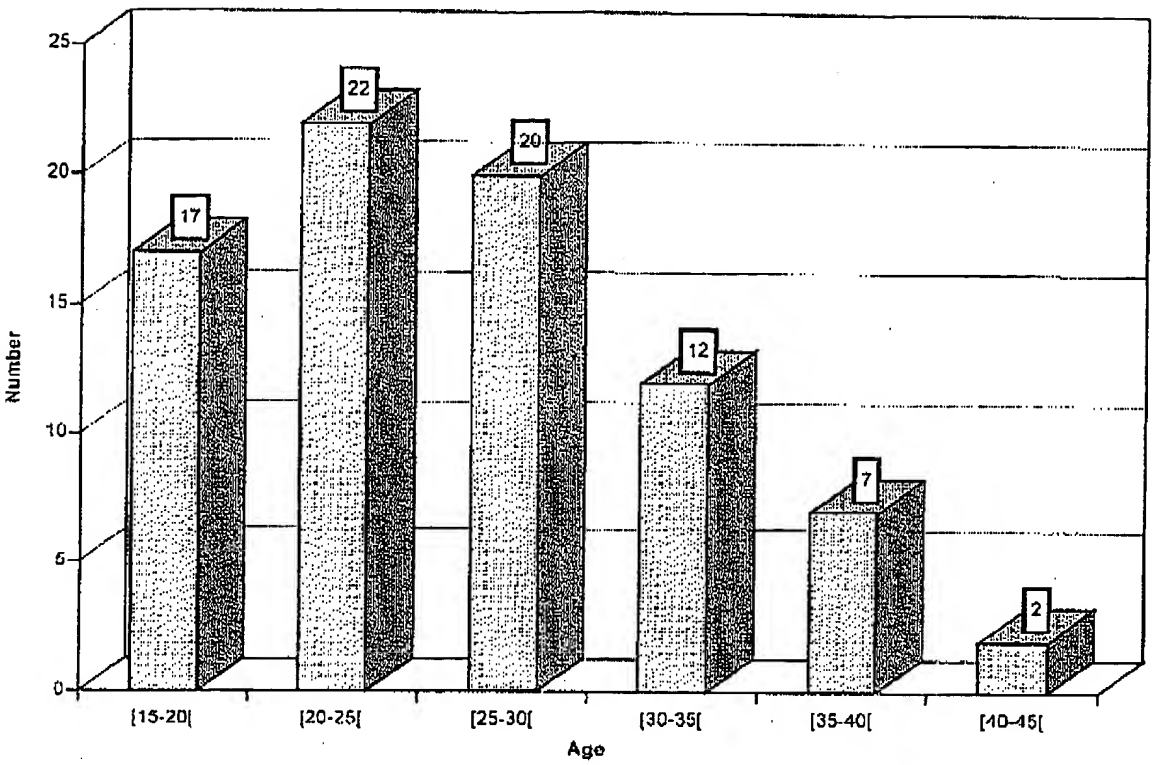

Fig. 1. Age distribution of the patients at the time of implantation.

frequently distorted and flattened, but no failures were reported in this area.

Histological examination of the Stryker® ligaments showed that these prostheses exhibited some degree of encapsulation characterized by collagenous granulomatous tissue. Collagen was observed penetrating the external knitted shell and, in most cases, between the yarns of the internal woven ribbons (Fig. 5). However, it rarely reached the center of the woven yarn bundle, which may have contained amorphous protein-like material, but no collagen. The textile structure of the ligament was generally well preserved except in those cases where the fibres in the external shell had become separated and frayed as a result of the healing process. A thick collagenous layer was observed between the knitted shell and the internal woven ribbons, and a chronic foreign body inflammatory response with macrophages and giant cells was noticed for all Stryker® explants. No severe inflammatory reaction was observed, and no direct correlation could be found between the extent of tissue ingrowth and the duration of implantation.

The SEM examination demonstrated that the fiber wear morphology of the external and the internal parts of this polyester ligament was similar. There was evidence of surface peeling as a result of yarn-on-yarn and yarn-on-bone abrasion. In the woven ribbons, axial splitting of the fibers was observed, suggesting some flexural and rotational fatigue (Fig. 6). No abrasion of the fibers were seen between the external shell and the internal ribbons. Some iatrogenic damage was also observed as some physicians reported problems in removing the prostheses during harvesting.

Proflex® ligament. This type of ligamentous prosthesis was usually received in two parts. Implantation more frequently involved using the over-the-top technique. In four specimens, the surgical procedure could not be determined because of the severe extent of damage (Fig. 7). Damaged zones located near the exit to the femoral and the tibial tunnels were observed with the through-the-condyle technique, whereas the exit to the tibial tunnel was the primary area affected when the over-the-top method was employed. The site of most ruptures for both techniques was at the distal end of the tibial tunnel and in the intra-articular zone.

Histological observations of the retrieved Proflex® ligaments revealed that the healing differed significantly from that of the Stryker® device. The Proflex® ligaments were not encapsulated by a thick granulomatous tissue, but instead, only a thin collagenous lining was observed (Fig. 8). As well as covering the outer surface of the ligament, this tissue capsule was found, in some cases, to penetrate through five or six layers of the 15-layer

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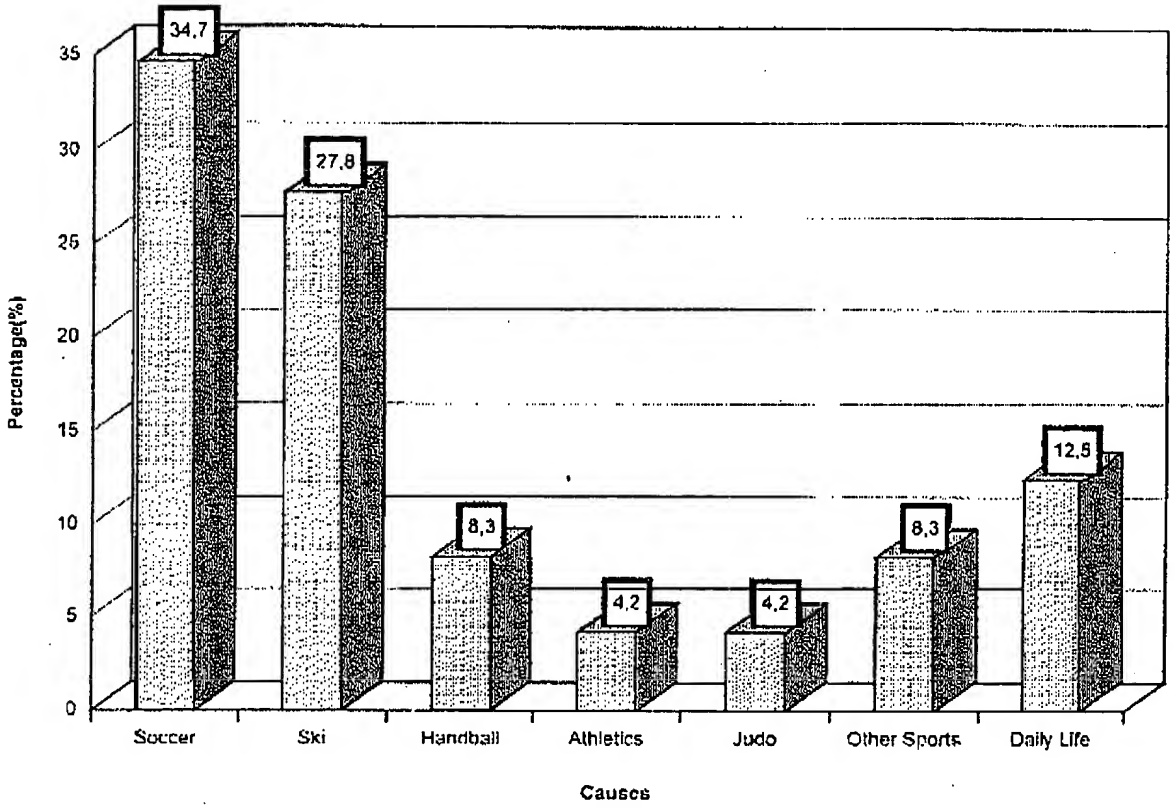

Fig. 2. Causes of rupture for the natural ACL.

braided structure. The infiltration of collagen into the external layers of the Proflex® ligament caused a loss of structural integrity as the braided polyester yarns became unravelled and separated into individual fibers within the tissue capsule. A chronic inflammatory reaction was observed and found to be similar to that of the Stryker® prosthesis. Again, no correlation was seen between the degree of healing and the duration of implantation.

The presence of damaged fibers with bushy ends in the central break zone of the prostheses was observed under SEM. Many fibers with surface peeling were observed on the outer shell and on the ribbons. This fiber wear morphology was attributed to yarn-on-yarn and yarn-on-bone abrasion. There was also some evidence of flexural and rotational fatigue as axial splitting was observed on many specimens (Fig. 9). These signs of damage were common to all prostheses and did not appear to be localized in only one location. There was no evidence of abrasion between the ribbons and the outer shell.

Lygeron® ligament: The preferred technique for the implantation of this ligament was the over-the-top technique. The ruptured prostheses were characterized by multiple breaks; thus, the explants arrived as numerous small pieces (Fig. 10). Consequently, it was impossible to locate the specific damaged zones, particularly when the outer shell was usually missing.

Healing of the Lygeron® ligament involved the development of a thick collagenous external capsule, which gradually grew thicker as the duration of the implantation increased. However, even after 3 yrs of implantation, the collagenous tissue did not penetrate further than the external woven shell and the first internal woven ribbon (Fig. 11). The moderate, chronic inflammatory reaction was found to be similar to that of the other polyester ligaments.

Some fibers with bushy ends were found within the ruptured regions. Fibers exhibiting axial splittings and surface peeling were common to all of the prostheses, suggesting that both flexural fatigue and surface abrasion had contributed to the failure (Fig. 12). As seen from the Stryker® and the Proflex® grafts, there was no evidence of deterioration due to abrasion between the outer shell and the internal ribbons, and in fact the extent of damage was similar in both layers.

SEM® ligament: The SEM® prostheses were invariably received in one single piece (Fig. 13). In all four cases, the through-the-condyle surgical technique has been used. Histologically, the SEM® ligament exhibited good

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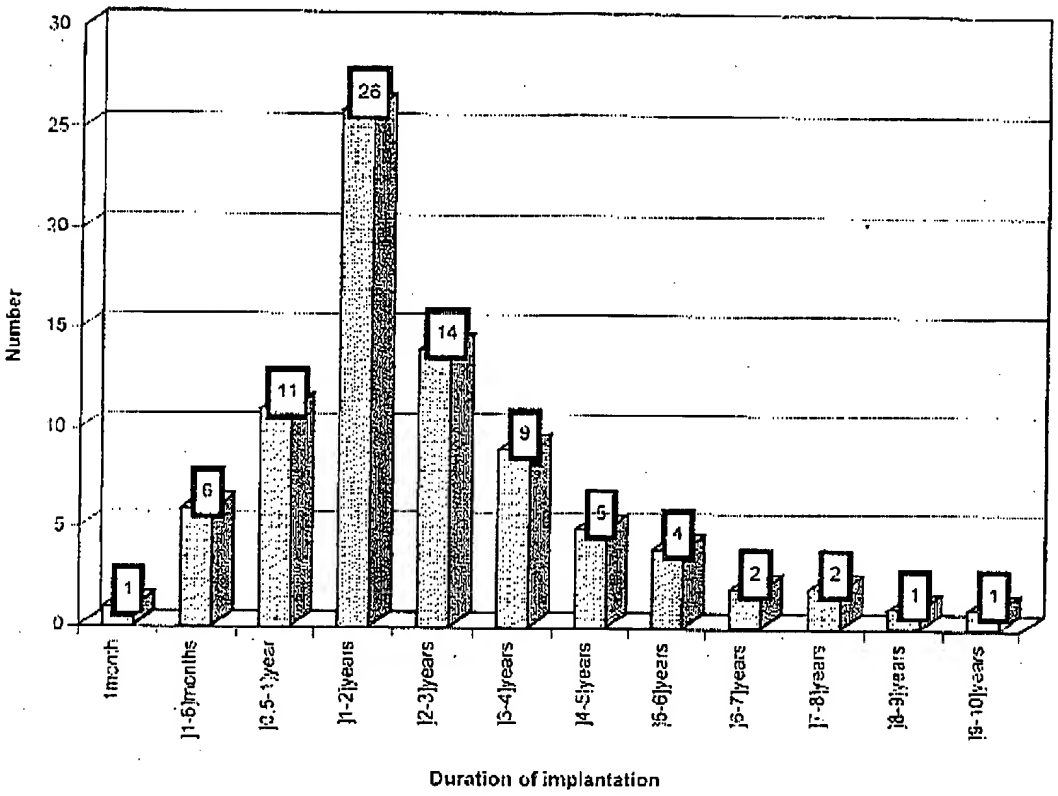

Fig. 3. Duration of implantation for the augmentation and replacement devices.

Table 2
Duration of implantation for ACL ligamentous prostheses made from polyester fibers

Commercial name	Duration (months)	Number received	Number datas
Stryker®	44.7 ± 33.4	28	19
Proflex®	24.2 ± 12.5	22	16
Lygeron®	36.1 ± 27.7	13	9
ABC Surgicraft® PET	31.5 ± 21.1	7	4
Ligastic®	59.3 ± 11.2	7	3
SEM®	27.4 ± 16.8	6	5
ABC Surgicraft® PET/C	18	2	1

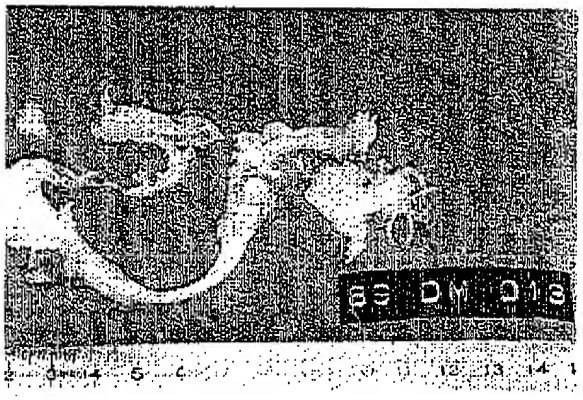

Fig. 4. Macroscopic view of a Stryker prosthesis (89lig013) after 43 months of implantation showing the rounded portion of the ligament which was attached to the femoral condyle, the frayed intra-articular portion and the segment inserted in the tibial tunnel.

encapsulation with penetration of collagenous tissue limited to the external braided shell only. Within this tubular structure, the infiltrating tissue was responsible for causing some yarn fraying and the separation of individual fibers (Fig. 14). A discrete chronic inflammatory response was noted. Fibers with surface peeling, caused by yarn-on-yarn and/or yarn-on-bone abrasion, were frequently observed. The presence of axial splittings was also noticed, suggesting flexural and/or rotational fatigue, and, in some sections, flattened fibres were also found (Fig. 15).

Ligastic® ligament: The Ligastic® prostheses were received in either one or several pieces. They had been

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Fig. 5. Light photomicrograph of a cross-section of an explanted Stryker prosthesis after 43 months of implantation showing dense penetration of collagenous tissue in the external envelope (arrow) and separation of the knitted structure into individual fibers (×125).

implanted using both the over-the-top and the through-the-condyle techniques. The cause of explantation was total rupture, which invariably occurred in the intra-articular zone. The shell layer was not available for a number of segments. The failure zone was characterized by the presence of fibers with bushy ends. Some surface peeling was also observed.

This particular device was manufactured in two different designs. The first, containing only a PET knitted structure, was an augmentation device, whereas the second, with its polyurethane outer shell, was designed to serve as a total ACL prosthesis. Only one out of the seven retrieved prostheses contained a polyurethane shell, which was surrounded by a thin collagenous capsule and which prevented the infiltration of tissue into the internal knitted structure. For the other six explants, the amount of external encapsulation was unpredictable, usually thin and occasionally absent. The collagenous tissue which was neither dense nor compact, infiltrated readily between the yarns and fibers of the knitted structure and easily reached the central core of the ligament. Again, the inflammatory reaction was chronic and moderate.

ABC Surgicraft® PET: These prosthetic ligaments were implanted using the over-the-top technique. They were received in one piece if their removal was not due to breakage, and in two pieces if the device had ruptured (Fig. 16). Failure invariably occurred proximal to the tibial condyle, and the damaged fibers in this zone were characterized by the presence of bushy ends.

The histological study revealed that the ABC Surgicraft® PET prostheses were well encapsulated by collagenous tissue, which penetrated to the core of the ligament between the 24 separate braids. Most of these prostheses also showed that the tissue was responsible for separating the yarns within a braid, but not the fibers within a yarn (Fig. 17). The inflammatory response was moderate and chronic, with macrophage and giant cells in contact with the fibers.

The SEM examination identified fibers with axial splitting and surface peeling which probably resulted from rotational and flexural fatigue and from surface abrasion.

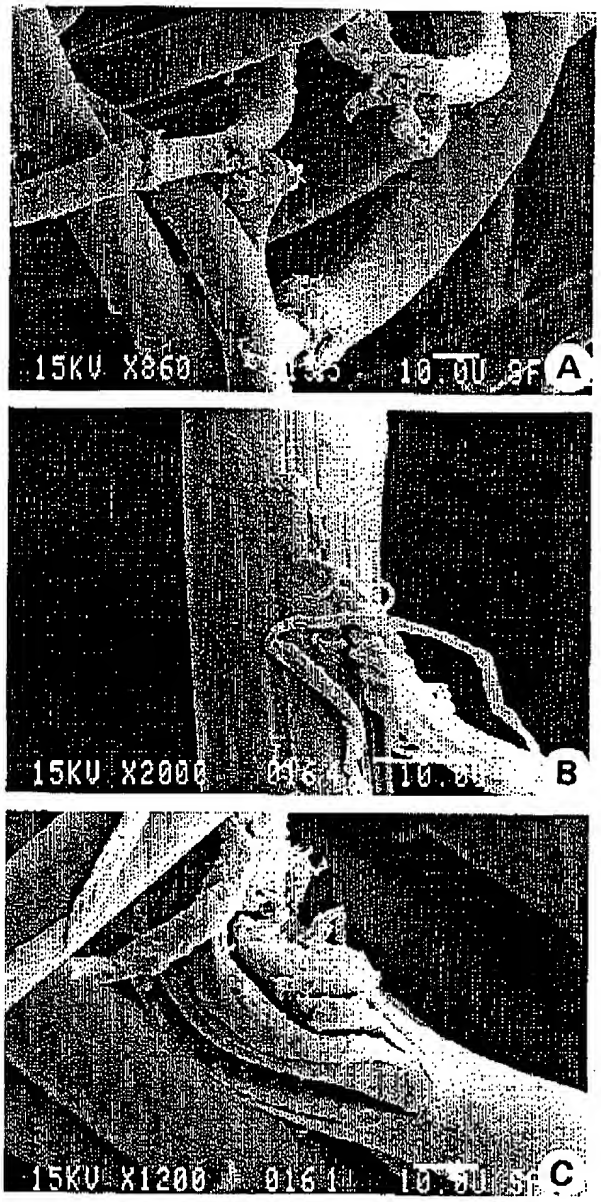

Fig. 6. Scanning electron micrographs of the polyester fibers from different explanted Stryker ligaments after cleaning. The fibers were generally flattened and appeared to be ruptured due to surface abrasion (A: × 860). Some fibers in the internal ribbon experienced surface peeling (B: × 2000). Axial splitting due to flexural and/or torsional fatigue was also observed within the core of the ligament (C: ×1200).

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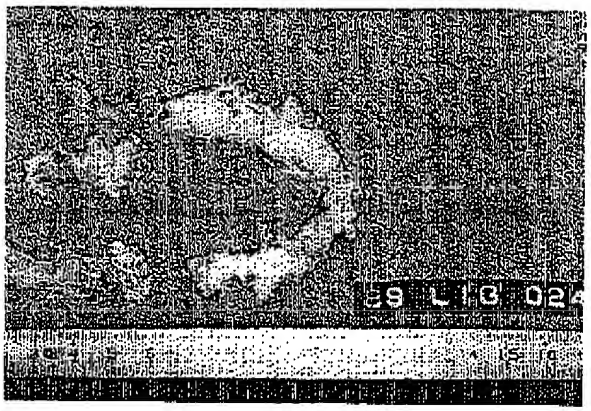

Fig. 7. Macroscopic view of one explanted Proflex ligament (89lig024) after 32 months of implantation. The break occurred in the central region of the ligament, and the section of prosthesis in the femoral condyle (left) was ruptured into two pieces.

Fig. 8. Light photomicrograph of a cross-section of an explanted Proflex device after 37 months of implantation. The extent of healing near the external surface of this multilayered structure is characterized by dense infiltration of collagen (C) causing expansion and separation of the polyester yarns into individual fibers (×125).

An excessive amount of surface peeling was observed among fibers near the fixation points.

ABC Surgicraft® PET/C: Both the through-the-condyle and the over-the-top techniques were used for the implantation of this device. With a limited number of specimens ($n = 2$), no conclusion could be made as to the exact zone of breakage nor to the healing sequence of these explants. The ruptured zone was characterized by the presence of fibers with bushy ends. The presence of surface peeling was also observed and may result from yarn-on-yarn or yarn-on-bone abrasion. This surface abrasion, as with the ABC Surgicraft® PET ligament, was more pronounced near the fixation points.

Fig. 9. Scanning electron micrographs of explanted Proflex prostheses after cleaning. The ruptured fibers in the external layer were characterized by extensive flattening and abrasion (A: ×1500). A bundle of fibers in the center of the ligament was severely abraded, exhibiting a fracture morphology referred to as 'bushy ends' (B: ×300). Multiple axial splitting was also observed in the central core of the Proflex prostheses likely induced by flexural and torsional fatigue (C: ×100).

3.3.2. *High-performance polyethylene (PHP) ligaments*

Braided PHP ligament: Six braided PHP ligaments were received in either one or two pieces. They were implanted between 1987 and 1991 for an average duration of 21.5 ± 3.5 months ($n = 2$). Four of them were

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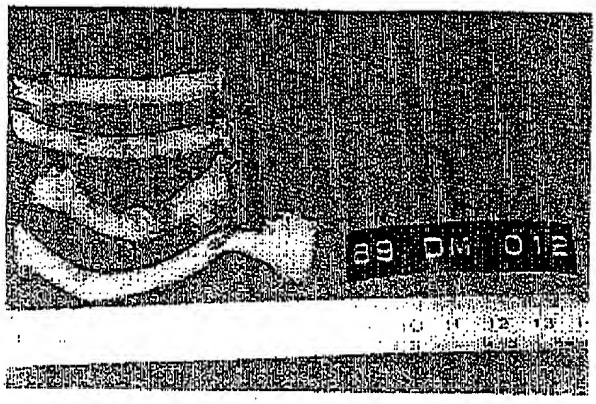

Fig. 10. Macroscopic view of a Lygeron ligament (89lig012) after 25 months of implantation showing multiple break zones which are difficult to reconstruct.

Fig. 11. Light photomicrograph of a cross-section of an explanted Lygeron prosthesis after 25 months of implantation showing the development of a collagenous external capsule (EC) which has penetrated only the first two woven layers of the multilayered structure (×125).

implanted using the through-the-condyle technique. One prosthesis was explanted because it ruptured at the exit to the femoral tunnel. The other five were excised due to synovitis.

Histogical examination revealed that the braided PHP ligaments were encapsulated by thick collagenous tissue which partly infiltrated the outer layers of the prosthesis. This collagen infiltration caused an expansion and separation of the multifilament yarns into individual fibers. A moderate, chronic inflammatory response was observed with numerous macrophages and giant cells.

Fiber wear morphology included evidence of surface peeling, probably due to surface abrasion and axial splitting, likely caused by flexural and torsional fatigue. However, it should be noted that the amount and extent of damage was limited.

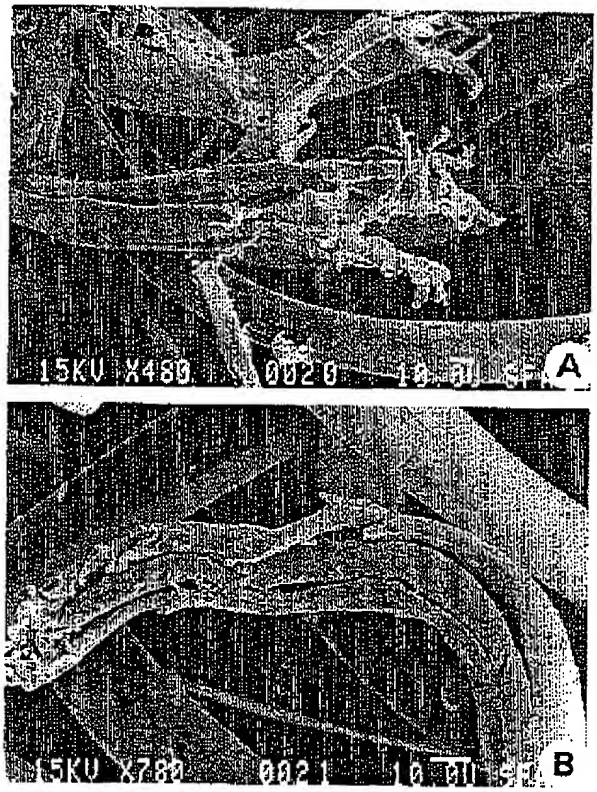

Fig. 12. Scanning electron micrographs of polyester fibers taken from the envelope of explanted Lygeron prostheses after cleaning showing a fracture morphology with multiple axial splitting and bushy ends (A: ×480). Fiber splitting due to flexural and torsional fatigue was also noted (B: × 780).

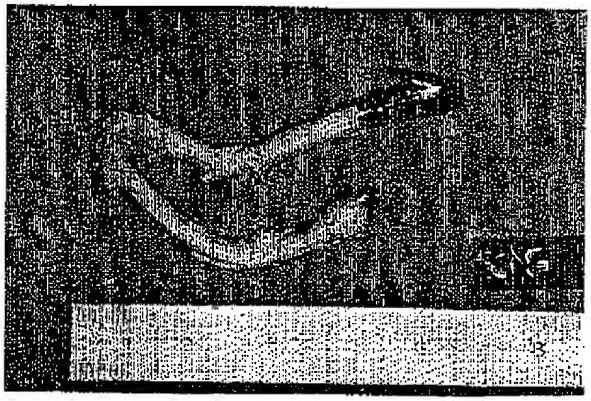

Fig. 13. Macroscopic view of an explanted SEM prosthesis (90lig003) after 11 months of implantation showing several exposed and abraded areas with significant tearing and fraying.

Raschel® or knitted PHP ligament: Six explanted Raschel® PHP prostheses with an average implantation time of 15.6 ± 9.6 months were examined. Four of them were

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Fig. 14. Light photomicrograph of a cross-section of an explanted SEM prosthesis after 11 months of implantation. The external layer of the ligamentous prosthesis is infiltrated by collagenous tissue which has separated individual fibers (×125).

implanted using the through-the-condyle technique, and all four were explanted due to rupture (Fig. 18). Histologically, the devices were encapsulated by thin collagenous tissue without any significant infiltration into the structure. A discrete to moderate, chronic inflammatory response was noted.

The SEM examination demonstrated that there were few signs of deterioration, except at the fixation points, where there was evidence of shear stress. In some areas, there was some surface peeling, and some twisted fibers, but overall there was little evidence of wear damage. One major problem reported with these PHP devices was synovitis.

3.3.3. *Expanded PTFE ligaments*

Gore-Tex® ligament: Three braided Gore-Tex® ligaments implanted for an average of 31.6 ± 2.8 months ($n = 2$) were installed using the through-the-condyle technique between 1987 and 1988 and explanted following rupture in the intra-articular zone (Fig. 19). Histological observations revealed that loose collagenous tissue surrounded the ligament and penetrated between individual fibers (Fig. 20). The extent of collagen infiltration was limited to the periphery of the device. This type of prosthetic ligament showed no evidence of an inflammatory reaction.

The SEM showed evidence of axial splitting, and some flattened fibers indicating that the failure mechanism was associated with flexural and rotational fatigue.

3.3.4. *Polyarylamide ligaments*

Ligaid® ligament: The Ligaid® ligaments were excised after an average implantation period of 18.7 ± 5.7 months ($n = 3$). One of these explants had been installed as an augmentation device, and the other three had been

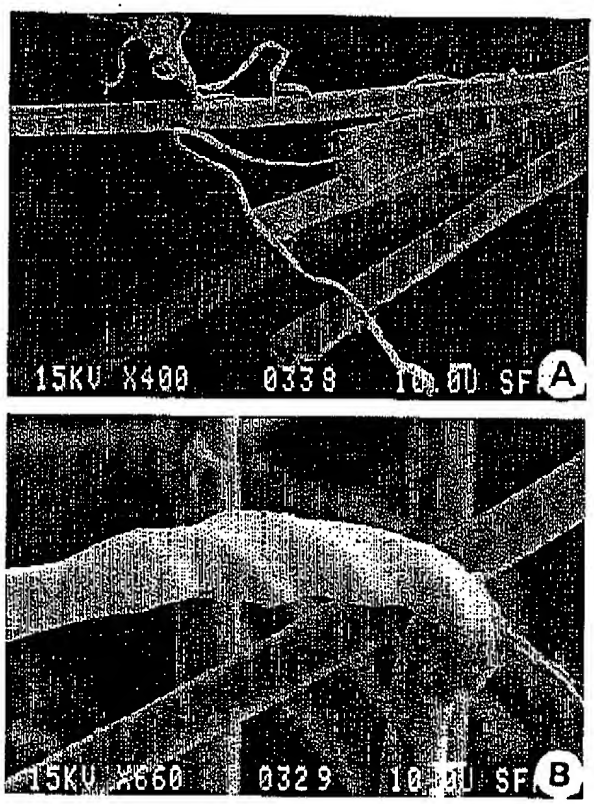

Fig. 15. Scanning electron micrographs of the polyester fibers from one SEM prosthesis after cleaning showing a flattened morphology and surface peeling in the damaged zones (A: ×400). Some fibers also experienced severe torsional rotation leading to axial splitting (B: ×660).

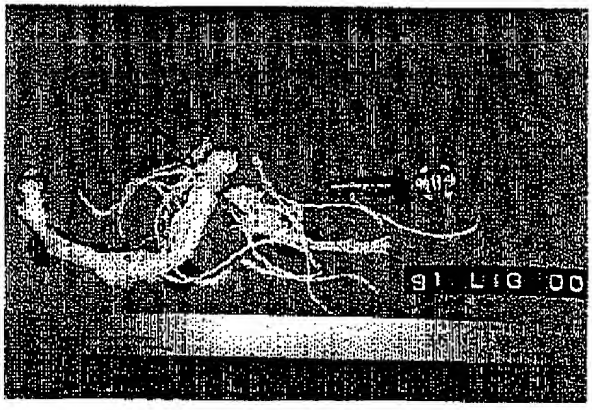

Fig. 16. Macroscopic view of an explanted ABC Surgicraft PET ligament (91lig004) after 48 months of implantation showing a distinct rupture in the intra-articular region with severe fraying of the braided structure.

used as ACL replacements. All of them were received in three pieces. Two of them had been implanted by using the through-the-condyle technique. There are no

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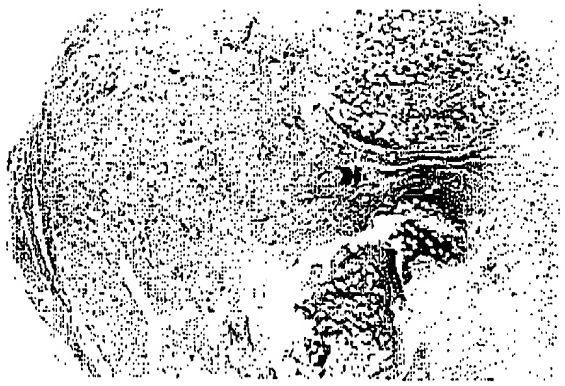

Fig. 17. Light photomicrograph of a cross-section of an explanted ABC Surgicraft PET prosthesis after 48 months of implantation. The collagenous tissue originating from a thick external capsule penetrated between the braids and occasionally between individual fibers (arrow). The black material observed within the braids was an amorphous proteinaceous across substance (×62).

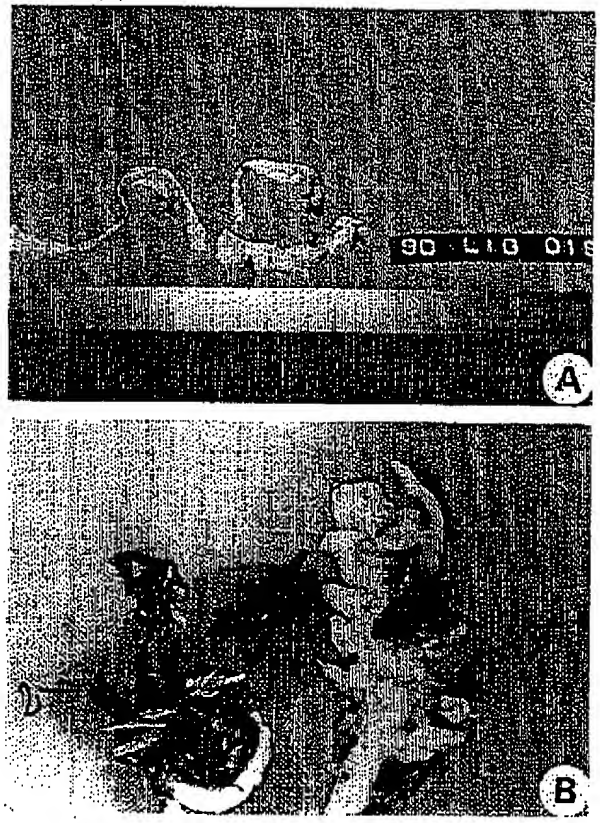

Fig. 18. Macroscopic view of an explanted PHP Raschel ligament (90lig019) after 6 months in vivo. It had ruptured into several pieces.

reported failures due to rupture among all four Ligaid® ligaments. The healing of the prosthesis showed good tissue encapsulation with collagen penetrating between the yarns and individual fibres (Fig. 21). The inflammatory response was discrete. Examination of the cleaned structure by SEM showed no signs of damaged fibers; in fact, the prosthesis and internal ribbons appeared to be well preserved.

4. Discussion

In the present study, 117 ACL grafts were examined after an average implantation time of 22 ± 13 months for the augmentation devices and 33 ± 25 months for the replacement prostheses. After reviewing the patients' medical reports, we were particularly interested in establishing whether the causes and mechanisms of failure were the same or different for the different types of ACL prostheses. We have found some similarities that may suggest common mechanisms for the loss of integrity of the various structures and failure of the ligamentoplasty.

First, there is no correlation between the duration of implantation and the degree of collagen infiltration. The ideal prosthesis has not only to be accepted by the body, but also has to promote collagen development, maturation, and orientation in and around the prosthesis in order to reproduce as closely as possible the natural ACL. All of the ACL prostheses examined histologically were infiltrated by collagen to different degrees. For the more porous knitted and braided structures, such as the Stryker®, Ligastic®, ABC® and Ligaid® prostheses, the collagenous tissue penetrated to the center of the device, whereas for the Proflex®, braided PHP and Raschel® PHP ligaments, collagenous tissue colonized only the outer layers. As for the Lygeron® and SEM® grafts, the extent of healing was limited to collagen ingrowth around the external shell, but not penetrating the tightly braided internal structure. In the case of the braided Gore-Tex® graft, the healing tissue was limited to the periphery of the ligamentous prosthesis. This poorer healing may be due in part to the PTFE polymer rather than the braided structure. For example, as arterial prostheses, PTFE grafts have been shown to exhibit an inferior healing capacity to polyester devices [25,26]. Finally, the development of a collagenous capsule wound in the Kennedy-LAD® augmentation device was limited to the outer layer only with insufficient collagen infiltration into the interior of the structure.

In several of these ACL prostheses (Proflex®, Stryker®, Ligastic®, Ligaid®), the collagen penetration into the textile structure caused the fibers to fray, swell and separate individually. This phenomenon subsequently contributed to increasing the level of abrasion against the bone and may help to explain why these devices experienced mechanical failure. In addition, the collagen appeared to

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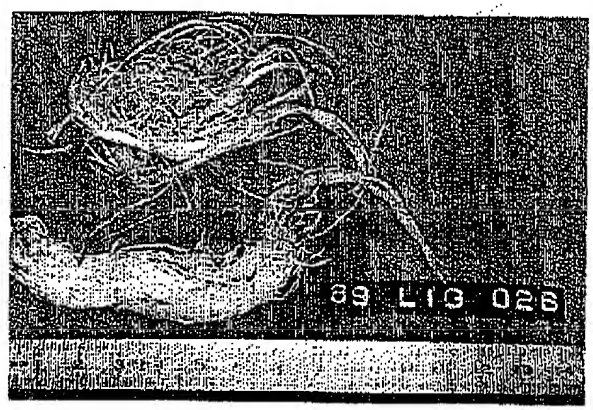

Fig. 19. Macroscopic view of an explanted Goretex prosthesis (89lig026) showing a break in the intra-articular zone with significant tearing and fraying of the ligamentous structure.

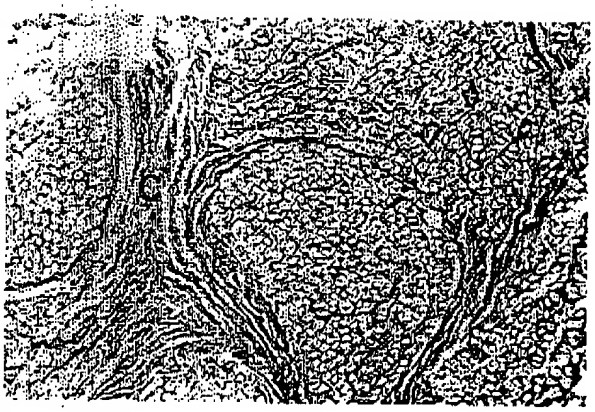

Fig. 21. Light photomicrograph of a cross-section of an explanted polyarylamide Ligaid prosthesis after 25 months of implantation showing the infiltration of collagenous tissue (C) between the yarns and fibers of this thin ligamentous structure (×125).

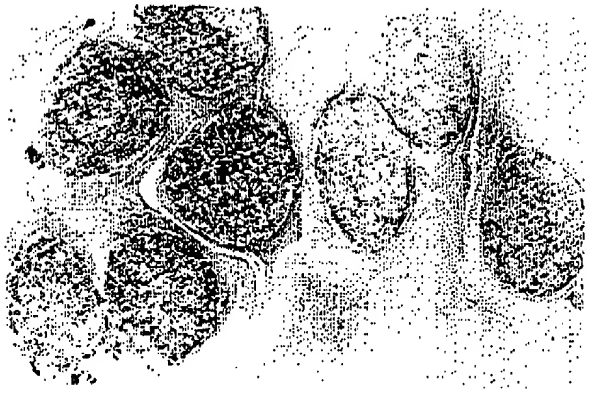

Fig. 20. Light photomicrograph of a cross-section of an explanted Goretex prosthesis after 22 months of implantation showing a loose and acellular collagenous tissue which penetrated between the PTFE fibers (P) (×62).

be more like accumulations of random scar tissue between the fibers rather than well-oriented collagen fibers capable of withstanding high mechanical loads. Even for those prostheses with good collagen infiltration, the collagen structure itself did not appear to be well organized and uniformly oriented like that formed in natural ligaments. Some studies have shown that these prostheses are colonized by type IV collagen, an immature collagen which does not provide any real mechanical support or reinforcement to the synthetic ligament [27,28]. As a result, this type of collagen infiltration may be more detrimental than beneficial to the biostability and bioendurance of these devices.

A second cause for the observed failure and rupture zones was the yarn-on-yarn and yarn-on-bone abrasion phenomena. This type of abrasion is characterized by surface peeling of the fibers, and its level of severity depends on the type of weave; the tighter the weave, the more the abrasion observed. The Stryker®, Proflex®, Lygeron® and Kennedy-LAD® devices suffered the most from this type of abrasion phenomenon. Three locations were particularly susceptible; namely, the proximal exit to the tibial tunnel in the intra-articular zone, around the condyle, and the distal exit to the femoral tunnel depending on whether the over-the-top or through-the-condyle technique was used. Limited signs of damage were observed with the Ligastic®, braided PHP and Gore-Tex® ligaments. In fact, wear phenomenon was generally absent in the ABC prostheses, except in the eyelet fixation region where the damage was more severe due to cyclic loading and the tightly woven design. This resulted in the prosthesis in some cases, being held by only one braid. This type of wear phenomenon was absent in the Raschel® PHP and Ligaid® devices.

A third mechanism contributing to the failure of ACL prostheses was flexural and rotational fatigue resulting from repeated flexions and extensions of the knee. This type of fiber fatigue is characterized by bushy ends and axial splittings. The phenomenon was observed in most of the retrieved prostheses, generally at the site of rupture. Only the Raschel PHP and Ligaid devices appeared to be immune to this type of structural failure.

In the 1990s most of the manufacturers gave up the production of these devices mainly because orthopedic surgeons were exasperated by their high rates of failure [23,29,30]. We believe that there is still a market for ligamentous prostheses. But before developing a new concept, it will be necessary to gain a better knowledge and understanding of the structure and properties of the natural ACL [27,31]. The healing of previous ACL prostheses was invariably incomplete: the tissue was neither

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oriented, nor did it provide any mechanical support or reinforcement. The problem of abrasion is one that is difficult to solve completely. Future improvements in ACL device performance may reside in designs that are able to protect these weak areas, such as the inclusion of a protective sleeve at the exits to the bone tunnels, and so increase the abrasion resistance. In addition, there is a need for more standardized installation techniques. According to Lemaire, there were more than 300 different surgical techniques reported during the 1980s alone, and they did not lead to significant improvements in success rates [32].

Further work therefore needs to focus on a number of issues, namely, standardized surgical protocols that avoid stress concentrations at fixation points and that reduce the wide variation in abrasion and loading points; introduction of new biomaterials that give a minimal (chronic) inflammatory response; and development of tissue engineering techniques that generate an optimally oriented and integrated tissue composite that will contribute to the load bearing capacity of the device.

5. Conclusion

We have identified a number of different phenomena that contributed to the failure of ACL prostheses. The textile structure of the device and the surgical technique used for its installation both appear to play a major role in influencing the healing response and the type of movement in the rehabilitated knee joint, as well as determining the long-term success of the ACL ligamentoplasty. The three most common mechanisms of failure involved (1) inadequate abrasion resistance of the yarns against themselves and osseous surfaces, (2) flexural and torsional fatigue of the fibers leading to axial splitting, and (3) structural changes and loss of integrity of the ligamentous prostheses due to unpredictable tissue infiltration. Future improvements lie in the development of innovative surgical techniques for implantation combined with a totally new concept for the biomaterials and prosthetic structure which will provide abrasion resistance and promote a completely healed and oriented tissue engineered device.

Acknowledgements

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